Correspondence

TO THE EDITOR, *British Journal of Venereal Diseases*

Mechanisms of selective toxicity of metronidazole and other nitroimidazole drugs

Sir,

I would like to comment on the article by D I Edwards[1] as several of his statements on the resistance of trichomonads to metronidazole disagree with the facts.

The strain of *Trichomonas vaginalis* isolated in Vienna in 1978 is not a unique finding.[2] Several other isolates with a reduced sensitivity to metronidazole have now been reported.[3 4] All these strains were isolated from treatment failures and all have shown in studies with mice in this laboratory a marked decrease in their sensitivity to metronidazole. The dose response was qualified on the basis of analogous data using strains from patients treated successfully with standard doses of metronidazole. The in-vivo resistant strains showed, under anaerobic conditions, a sensitivity similar to that of sensitive strains in-vivo. Thus these strains behaved identically to a "truly resistant" strain of *Tritrichomonas foetus* made resistant to metronidazole in mice by drug pressure.[5] These findings indicate that the anaerobic sensitivity tests used were not reliable. Trichomonads with proved metronidazole resistance showed false "normal" sensitivity under anaerobic conditions.

It is well known that under aerobic conditions the minimum lethal concentration (MLC) of metronidazole for trichomonads is increased. This was shown in the papers for both sensitive and resistant strains, but MLCs for strains exhibiting resistance in vivo were markedly increased when O_2 was present in the cultures.[4 6]

In summary, we believe that these data provide strong evidence that metronidazole-resistant strains of *T vaginalis* do exist and that results from aerobic assays showing markedly increased MICs, compared with sensitive reference strains, are of clinical importance. This conclusion is supported by another recent paper.[7]

I would gladly supply Dr Edwards with resistant strains to test in his own laboratory.

Yours faithfully,

J G Meingassner

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References

1. Edwards DI. Mechanisms of selective toxicity of metronidazole and other nitroimidazole drugs. *Br J Vener Dis* 1980;**56**: 285-90.
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3. Forsgren A, Forssman L. Metronidazole-resistant *Trichomonas vaginalis*. *Br J Vener Dis* 1979;**55**:351-3.
4. Müller M, Meingassner JG, Miller WA, Ledger WJ. Three metronidazole-resistant strains of *Trichomonas vaginalis* from the United States. *Am J Obstet Gynecol* 1980; **138**:808-12.
5. Meingassner JG, Mieth H, Czok R, Lindmark DG, Müller M. Assay conditions and the demonstration of nitroimidazole resistance in *Tritrichomonas foetus*. *Antimicrob Agents Chemother* 1978;**13**:1-3.
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7. Smith RF, Domenico di A. Measuring the in-vitro susceptibility of *Trichomonas vaginalis* to metronidazole. *Sex Transm Dis* 1980;**7**: 120-4.

** This letter has been shown to Dr Edwards, whose reply is printed below. ED, *BJVD*.

I welcome Dr Meingassner's comments on *T vaginalis* resistance to metronidazole and other nitroimidazoles. I agree entirely that truly resistant *T vaginalis* exist, but it is only comparatively recently that this has been conclusively demonstrated and much of the credit must go to Dr Meingassner's laboratory. The evidence is contained in those references quoted in his letter, only two of which, however, were available to me at the time of writing the review.

The most important findings of such studies have been the documentation that nitroimidazole resistance appears to involve aerobic tolerance of *T vaginalis* to the drugs rather than an anaerobic one. This raises questions as to the O_2 tension and redox levels existing in the vagina in both normal and infected states. Such data would be valuable in correlating parameters of the vaginal environment to resistance levels found in aerobic and anaerobic culture of *T vaginalis* together with the O_2 tension and redox levels.

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TO THE EDITOR, *British Journal of Venereal Diseases*

Regional variations in the STD clinic service in England and Wales

Sir,

The aims of Houghton *et al*[1] in their paper on the regional variations in the sexually transmitted disease clinic service in England and Wales seem to me rather obscure. I doubt that anyone has ever believed that sexually transmitted diseases are distributed geographically in proportion to total population so that it is difficult to accept that relating service to crude population has any conceivable use.

Surely the most practical way of distributing resources is for supply to follow demand, although no one would deny that considerable latent demand must exist. This is largely governed by local attitudes and quality of service, but still some patients will travel long distances for treatment by choice and not because they have no alternative.

Most of these points are admittedly picked up in the discussion, where the authors finally admit that their conclusions are of limited use for planning purposes without suggesting what other purpose they might serve in a clinical scientific journal. Perhaps they will form a basis for the "special descriptive studies" on which the reader is left to ponder.

Yours faithfully,

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Reference

1. Houghton GM, Adler MW, Belsey, EM. Regional variations in the sexually transmitted disease clinic service in England and Wales. *Br J Vener Dis* 1981;**57**:70-6.

Notice

International conference on psychosexual medicine

The Institute of Psychosexual Medicine will hold their first international conference in Brighton (England) from 7 to 10 July 1982. For further information apply to: IPM Conference Secretariat, Caroline Roney Medical Conference Organisers, 100 Park Road, London NW1 4RN: telephone 01-723 6722.